REMARKS

Claims 51-58 are pending in the subject application. By this Amendment, applicants have canceled claim 52 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in the future, and have amended claims 51 and 53-57.

The amendments to claim 51 involve formatting changes and the incorporation of the subject matter of now-canceled claim 52. The amendments to claims 53-57 delete references to now-canceled claim 52. Thus, applicants maintain that these amendments do not raise any issue of new matter. Accordingly, applicants respectfully request that the Examiner enter this Amendment. Upon entry of this Amendment, claims 51 and 53-58, as amended, will be pending and under examination.

Double Patenting Rejections

1. Over Claims 15 and 16 of U.S. Serial No. 09/412,284 (now U.S. Patent 6,972,126)

The Examiner provisionally rejected claims 51-58 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 15 and 16 of copending U.S. Serial No. 09/412,284. The Examiner alleged that although the conflicting claims are not identical, they are not patentably distinct from one another. The Examiner alleged that claims 51-58, and copending claims 15 and 16, are drawn to an antibody that is specific for the CCR5 receptor. The Examiner also stated that claims 51-58 differ from copending claims 15 and 16 in that claims 51-58 fail to recite a number of properties listed in the copending claims. The Examiner asserted that it would, however, have been *prima facie* obvious to omit these features given that they fail to structurally distinguish the antibody of claims 51-

58.

In response, applicants submit a Terminal Disclaimer attached hereto as **Exhibit A**. Applicants note that U.S. Serial No. 09/412,284 is now U.S. Patent No. 6,972,126, issued December 6, 2005. Accordingly, the attached Terminal Disclaimer refers to U.S. Patent No. 6,972,126, rather than to U.S. Serial No. 09/412,284.

2. Over U.S. Serial No. 09/852,236 in view of Young et al.

The Examiner also provisionally rejected claims 51-58 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 18 and 20 of copending U.S. Serial No. 09/852,236 in view of Young et al. (U.S. Patent No. 5,449,608, issued September 12, 1995). The Examiner alleged that although the conflicting claims are not identical, they are not patentably distinct from one another. The Examiner noted that claims 51-58, and copending claims 18 and 20, are drawn to an agent that binds the CCR5 receptor. According to the Examiner, claims 51-58 differ from copending claims 18 and 20 in that the copending claims fail to require the agent to be an antibody. The Examiner stated that Young et al., however, teach an antibody directed against a virus-associated cell surface protein (citing col. 2, lines 66-67, and col. 3, lines 1-2). The Examiner asserted that it would have been obvious to modify copending claims 18 and 20 to include an antibody because Young et al. teach that anti-receptor antibodies provide a useful means for preventing viral attachment to target cells. The Examiner noted that claim 21 of copending Application Serial No. 09/852,236 was not included in this rejection even though it limits claim 20 by requiring an antibody. The Examiner explained that this is because it appears that claim 21 was intended to depend from claim 19 (claim 21 refers to the ligand of claim 19) which is not

an obvious variant of claims 51-58.

In response, applicants respectfully traverse this rejection. Applicants note that U.S. Serial No. 09/852,236, on which the present rejection is based, is an abandoned application, entitled "Pager with both POCSAG and FLEX systems," and naming Tsung-Hsin Chang et al. as inventors. This U.S. Serial No. 09/852,236 is unrelated to the subject application. Applicants understand that the Examiner's rejection is based on U.S. Serial No. 09/852,238, filed May 9, 2001, entitled "Uses of a chemokine receptor for inhibiting HIV-1 infection." However, applicants note that U.S. Serial No. 09/852,238 has been abandoned, thereby rendering the present ground of rejection moot in so far as that specific application is concerned.

3. Over U.S. Serial No. 10/371,483

The Examiner also provisionally rejected claims 51-58 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-5, 18 and 31 of copending U.S. Serial No. 10/371,483. The Examiner alleged that although the conflicting claims are not identical, they are not patentably distinct from one another. The Examiner alleged that claims 51-58 and copending claims 1-5, 18 and 31 are both drawn to an antibody that is specific for the CCR5 receptor. According to the Examiner, claims 51-58 differ from copending claims 1-5, 18 and 31 in that copending claims 1-5, 18 and 31 require specific expression products from a number of plasmids. The Examiner asserted that it would, however, have been obvious to omit the specific sequences required by copending claims 1-5, 18 and 31. The Examiner further asserted that one skilled in the art would readily recognize that vaccinating animals with the CCR5 polypeptide would provide an easier method for producing anti-CCR5 antibody than the method used to produce the antibody of the

copending claims. The Examiner thus concluded that it would therefore have been obvious to omit the specific sequences required by copending claims 1-5, 18 and 31 in order to simplify the production of the CCR5 antibody.

In response, applicants respectfully traverse this obviousness-type double patenting rejection. Without conceding the correctness of the Examiner's position, applicants note that this is a provisional rejection over the U.S. Serial No. 10/371,483 which is not an allowed application. Accordingly, if the claims of the subject application are otherwise allowable, the provisional double patenting rejection should be withdrawn and the claims in the subject application should be allowed and issued, where upon the claims of the U.S. Serial No. 10/371,483 could be assessed as to whether an obviousness-type double patenting rejection over the subject application would be warranted which applicants maintain would not be the case.

Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 51-58 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Examiner stated that claims 51-58 are indefinite in the recitation of "[a]n isolated antibody *capable of binding* ... and inhibiting". The Examiner also stated that this language fails to clearly indicate whether in fact the isolated antibody has the recited binding and inhibiting properties, and requested appropriate correction.

In response, applicants, without conceding the correctness of the Examiner's position, have amended claim 51 to recite an isolated antibody which binds to a human CCR5 chemokine receptor on the

surface of a CD4+ cell and inhibits HIV-1 infection of such CD4+ cell. As amended, claim 51 does not recite the phrase "capable of binding ... and inhibiting", and clearly indicates that the isolated antibody has the recited binding and inhibiting properties. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejections Under 35 U.S.C. §112, First Paragraph

Enablement

The Examiner rejected claims 51-58 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which the invention pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

The Examiner stated that undue experimentation is defined by the following factors: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure (citing *In re Wands*, 858 F.2d at 737, 8 USPQ2d 1400, 1404).

The Examiner stated that the state of the art as of applicants' priority date shows that *in vivo* therapy for inhibiting HIV infection generally relied on nucleoside analogs such as AZT (citing FASEB J. [September 1995] 9, 1157-1163). The Examiner also stated that an HIV treatment based on an anti-chemokine

receptor antibody was neither suggested nor practiced in the art. The Examiner further stated that, at most, the art demonstrated that some beta-chemokines were capable of disrupting HIV infection *in vitro* (citing Science [1995] 270, 1811-1815). Thus, the Examiner concluded that one skilled in the art could not easily predict how to suppress HIV infection *in vivo* using a therapy based on anti-chemokine receptor antibodies.

The Examiner stated that the art that came closest to suggesting such a therapy showed that RANTES, MIP-1 beta and MIP-1 alpha had some ability to disrupt the infection of CD4+ clones *in vitro* using laboratory strains of HIV (*id.*). The Examiner also stated that these effects were, however, inconsistent (citing, e.g., page 1813, ¶1, and Fig. 2B) and failed to suggest that the use of anti-chemokine receptor *antibodies* would inhibit HIV infection *in vivo*. The Examiner further stated that, based on the unpredictability of using anti-chemokine receptor antibodies to inhibit HIV infection *in vivo*, one skilled in the art would have to rely heavily on the specification in order to practice the claimed invention. The Examiner asserted that the specification fails, however, to provide adequate direction for reducing the claimed antibody to practice.

The Examiner also stated that while the specification makes passing references to an anti-chemokine receptor antibody (citing page 12, lines 10-13, and page 17, line 5), the majority of the specification relates to CCR5 antagonists that compete with gp120 for the CCR5 receptor. The Examiner further stated that this also applies to applicants' working examples which show the effect of chemokines and non-chemokine peptide antagonists on HIV attachment and entry *in vitro*. The Examiner asserted that the specification does not teach an antibody that is specific for the chemokine receptor, let alone an antibody that is capable of

inhibiting HIV infection *in vivo*.

In addition, the Examiner alleged that applicants' specification also fails to teach the motifs and/or regions of the CCR5 receptor that are involved in supporting HIV attachment and entry. The Examiner alleged that, given the unpredictability of using anti-chemokine receptor antibodies noted above, and the specification's failure to teach or suggest such an antibody, practicing the invention as claimed would require undue experimentation.

The Examiner alleged that the specification also fails to enable the range of chemokine receptor antibodies that are claimed. The Examiner stated that the claims are drawn to an antibody that recognizes any human chemokine receptor on the surface of a CD4+ cell that inhibits the infection of CD4+ cells by HIV. The Examiner stated that applicants have, however, only disclosed the CD4+ CCR5 receptor as capable of modulating HIV infection. The Examiner further stated that applicants have not disclosed any other chemokine receptors that modulate HIV infection of CD4+ cells. The Examiner asserted that the claims therefore also lack enablement for the range of chemokine receptor antibodies presently claimed.

In response, applicants first note that the now-claimed invention provides an isolated antibody which binds specifically to a human CCR5 chemokine receptor on the surface of a CD4+ cell and inhibits HIV-1 infection of such CD4+ cell. Thus, the now-claimed invention is not drawn to "an isolated antibody that recognizes any human chemokine receptor on the surface of a CD4+ cell" (emphasis added), nor to a "range of chemokine receptor antibodies." Applicants also note that the claims are directed to an antibody not a method of treatment. Therefore, the

Examiner's comments concerning using an antibody for *in vivo* treatment are misplaced and would only be applicable to a method of treatment claim not presented here. Applicants further note that the complete nucleotide sequence of the CCR5 gene, and the deduced amino acid sequence of the CCR5 receptor, were in the public domain prior to the April 2, 1996 effective filing date of the subject application, having been published by Samson et al. on March 19, 1996. See Samson et al. (1996) Molecular cloning and functional expression of a new human CC-Chemokine receptor gene, Biochem. 35: 3362-3367; cited as Reference 22 on page 38 of the specification, and listed as Reference LL in an Information Disclosure Statement filed August 9, 2001 in connection with the subject application. Moreover, Samson et al. describe the expression of a functional CCR5 receptor on the surface of mammalian cells. Applicants note that the specification explicitly teaches at page 22, lines 27-30, that "[f]ollowing expression of the receptor, monoclonal and polyclonal antibodies are prepared and tested for ability to inhibit infection by a panel of HIV-1 isolates". Applicants maintain that, given public knowledge of the CCR5 receptor sequence and the successful expression of functional CCR5 receptor on the surface of a cell, the preparation of antibodies that bind to a CCR5 receptor on the surface of a cell required only routine experimentation as of the effective filing date of the subject application. Applicants assert that there was therefore no requirement to provide in the specification a detailed description of what are routine methods for preparing such antibodies against CCR5 expressed on the surface of a cell since, to satisfy the enablement requirement, "a patent need not teach, and preferably omits, what is well known in the art." (Emphasis added) *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). See also *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991) ("The specification need not disclose what is well known in

the art"). Accordingly, applicants maintain that the omission of a detailed protocol for such a routine procedure does not negatively impact the enablement of the claimed invention.

In addition, applicants note that the specification provides a routine fluorescence resonance energy transfer (RET) assay for identifying agents that inhibit fusion of HIV-1 to CD4+ cells (see, *inter alia*, page 17, line 33 to page 18, line 15, and page 18, lines 26-34). Thus, applicants maintain that, based on the content of the prior art and the disclosure set forth in the specification, one of ordinary skill in the art could readily prepare an antibody that binds to a human CCR5 chemokine receptor on the surface of a CD4+ cell and inhibits HIV-1 infection of such CD4+ cell, as claimed, using only routine experimentation.

In view of the preceding remarks, applicants disagree with the Examiner's assertions on page 6 of the Office Action that the specification makes only passing references to an anti-chemokine receptor antibody (citing page 12, lines 10-13, and page 17, line 5), and that the specification does not teach an antibody that is specific for the chemokine receptor, let alone an antibody that is capable of inhibiting HIV infection *in vivo*. Accordingly, applicants respectfully direct the Examiner's attention to the disclosures in the specification relating to the cloning of the CCR5 receptor (see page 33, lines 3-17, and page 34, lines 23-26), the expression of functional CCR5 in human CD4-expressing cell lines (see page 34, lines 27-30), experimental data indicating that the CCR5 receptor is the chemokine receptor that mediates fusion of CD4+ cells to primary HIV-1 strains (see, *inter alia*, page 31, lines 8-11, and page 35, line 19 to page 36, line 16), the teaching that following expression of the receptor, monoclonal and polyclonal antibodies are prepared and tested for ability to inhibit infection by a

panel of HIV-1 isolates (page 22, lines 27-30), and the use of the RET assay for screening agents to identify those that inhibit HIV-1 infection of cells (see, *inter alia*, page 17, line 52 to page 18, line 15, and page 18, lines 26-34). Moreover, as noted above, the *in vivo* effectiveness of the claimed antibody is not relevant to whether the claim to the antibody is enabled.

Regarding the Examiner's reference to the *Wands* factors, applicants note that "it is not necessary that a court review all of the *Wands* factors to find a disclosure enabling. They are illustrative, not mandatory. What is relevant depends on the facts ..." See *Amgen v. Chugai Pharmaceutical* 927 F.2d 1200, 1213 (Fed. Cir. 1991). Based on the considerations set forth below, applicants assert that more than a sufficient number of the *Wands* factors are satisfied to establish that the specification enables the claimed invention.

1. Breadth of claims: Applicants maintain that the claims, as amended, are not duly broad since they refer to an antibody which binds specifically to a specific cell surface receptor, i.e. a human CCR5 receptor (i.e., not to a range of chemokine receptors) on the surface of a CD4+ cell and inhibits HIV-1 infection of such CD4+ cell.

2. State of prior art: The art taught the sequence of the CCR5 receptor and its functional expression on the surface of mammalian cells. Applicants maintain that, given the content of the prior art combined with the specification of the subject application, the preparation of antibodies against the human CCR5 receptor expressed on the surface of a CD4+ cell would have been routine, as of the effective filing date of the subject application.

3. Level of skill in the art: The level of skill in the biotechnology arts is generally acknowledged to be very high. See, for example, *Enzo Biochem, Inc. v. Calgene, Inc.* 188 F.3d 1362, (Fed. Cir. 1999):

> [T]he district court determined that a person of ordinary skill in the art would be 'a junior faculty member with one or two years of relevant experience or a postdoctoral student with several years of experience,' *see Enzo,* 14 F.Supp.2d at 567, and we discern no clear error in this determination.

4. Quantity of experimentation needed: Applicants note that *Wands* itself clarifies that the relevant factor in assessing enablement is not the amount of experimentation required to practice an invention, but whether the experimentation required is routine. See *In re Wands*, 8 U.S.P.Q.2d 1400, 1404:

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. ... The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, ... (emphasis added)

Applicants reiterate that, based on the disclosures in the specification coupled with information known in the art, one skilled in the art could readily make antibodies against the human CCR5 receptor expressed on the surface of a CD4+ cell transfected with a cloned CCR5 gene, and screen the antibodies thus prepared using the RET assay to identify those that inhibit HIV-1 infection of such CD4+ cell.

Accordingly, applicants maintain, for the above reasons, that the specification teaches one skilled in the art how to make and use,

without undue experimentation, an antibody which binds to a human CCR5 chemokine receptor on the surface of a CD4+ cell and inhibits HIV-1 infection of such CD4+ cell.

Applicants also disagree with the Examiner's statement that the specification fails to teach the motifs and/or regions of the CCR5 receptor that are involved in supporting HIV attachment and entry. In this regard, applicants note that the CCR5 receptor is a membrane-bound protein belonging to a well characterized G-protein-linked superfamily of receptors containing seven membrane-spanning domains. See the specification at page 25, lines 6-13. This superfamily included, at the time of the identification of the CCR5 receptor, four previously characterized chemokine receptors. See Samson et al. (1996), abstract, *Supra*. By homology to these previously characterized chemokine receptors, the extracellular, transmembrane and intracellular regions of the CCR5 receptor can be readily ascertained. Indeed, prior to the effective filing date of the subject application, Samson et al. (1996) had identified seven transmembrane domains, the N-terminal extracellular domain and three extracellular loops in CCR5 (see page 3364, Fig. 1 and right col.). Applicants note that HIV-1 necessarily binds to regions of CCR5 exposed on the surface of a cell, i.e., to extracellular regions. Applicants maintain, therefore, that as of the effective filing date of the subject application, the motifs and/or regions of the CCR5 receptor that are involved in supporting HIV attachment and entry were known to be located in the extracellular regions of CCR5, which regions had been previously publicly described.

Based on the foregoing remarks, applicants maintain that the specification as filed enables one skilled in the art to make and use the invention recited in the now-pending claims without undue

experimentation. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Written Description

The Examiner rejected claims 51-58 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner stated that applicants' claims lack adequate written description for the following two reasons.

First, the Examiner alleged that applicants have not disclosed a representative number of chemokine receptors that are capable of modulating HIV infection. The Examiner also stated that applicants' claims are drawn to an antibody that is specific for "a human chemokine receptor on the surface of a CD4+ cell ..." The Examiner further stated that applicants have, however, only disclosed the CCR5 receptor as being involved in HIV infection. The Examiner concluded that the claims therefore lack written description for a representative number of CD4+ chemokine receptors.

Second, the Examiner alleged that the claims lack written description for a representative number of antibodies that are specific for CD4+ chemokine receptors. The Examiner alleged that, not only does the specification lack support for a representative number of chemokine receptors, it also lacks support for a representative number of antibodies that are

specific for these receptors. The Examiner further alleged that the specification does not disclose the chemokine receptor (i.e., CCR5) epitopes with adequate detail to allow one skilled in the art to conclude that applicants possessed the range of antibodies presently claimed, and there is no disclosure of the extracellular motifs and/or regions of CCR5 chemokine receptor regions that would allow an antibody to prevent coreceptor activity. The Examiner stated that disclosure of the regions involved in the binding of a chemokine receptor ligand is also lacking. The Examiner also asserted that, based on this lack of disclosure, one skilled in the art could not reasonably conclude that the inventors possessed the range of antibodies presently claimed. The Examiner thus concluded that the claims lack written description for a representative number of anti-chemokine receptor antibodies.

In response, applicants respectfully traverse this rejection. Applicants again note that the claims, as amended herein, refer to an isolated antibody which binds specifically to a human CCR5 chemokine receptor on the surface of a CD4+ cell and inhibits HIV-1 infection of such CD4+ cell. Applicants further note that the specification discloses that the CCR5 receptor is the chemokine receptor that mediates fusion of CD4+ cells to primary HIV-1 strains (see, *inter alia*, page 31, lines 8-11, and page 35, line 19 to page 36, line 16). Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

In response to the Examiner's assertion that the claims lack written description for a representative number of antibodies that are specific for CD4+ chemokine receptors, applicants reiterate that an antibody which specifically recognizes the CCR5 receptor is now being claimed. Moreover, applicants maintain

that the specification conveys to one skilled in the art that applicants were in possession of the claimed invention at the time the application was filed for the following reasons: (1) the specification clearly discloses an isolated antibody which is prepared against a human CCR5 chemokine receptor on the surface of a CD4+ cell and inhibits HIV-1 infection of such CD4+ cell, as recited in independent claim 51 (see, *inter alia*, page 11, lines 32-34; page 12, lines 10-12; page 22, lines 27-30); (2) the complete nucleotide and amino acid sequence of the CCR5 gene and receptor, respectively, were in the public domain prior to the effective filing date of the subject application (see Samson et al. [1996]); (3) the specification discloses (a) the identification of the human CCR5 receptor as the chemokine receptor that mediates fusion of CD4+ cells to primary HIV-1 strains (see, *inter alia*, page 31, lines 8-11, and page 35, line 19 to page 36, line 16), (b) the cloning of the human CCR5 receptor (page 33, lines 3-17, and page 34, lines 23-26), and (c) the expression of functional human CCR5 in human CD4-expressing cell lines (page 34, lines 27-30); (4) one skilled in the art would understand that disclosing the sequence of the human CCR5 receptor and expressing this receptor on the surface of a CD4+ cell effectively describes antibodies that bind the receptor on the surface of the cell since such antibodies are readily generated by routine experiments (see page 12, lines 12-13, and page 22, lines 27-30); and (5) the specification describes a routine RET assay for screening antibodies prepared against the human CCR5 receptor on the surface of the cell for their ability to inhibit fusion of HIV-1 to CD4+ cells, thereby inhibiting HIV-1 infection of CD4+ cells (see, *inter alia*, page 17, line 33 to page 18, line 15, and page 4, lines 8-13).

Applicants refer to the Examiner's assertions on pages 7-8 that the specification does not disclose CCR5 epitopes with adequate

detail to allow one skilled in the art to conclude that applicants possessed the range of antibodies presently claimed, and there is no disclosure of the extracellular motifs and/or regions of CCR5 chemokine receptor regions that would allow an antibody to prevent coreceptor activity.

In response, applicants respectfully disagree with these assertions. Applicants note that the extracellular domains of the human CCR5 receptor were publicly disclosed prior to the effective filing date of the subject application. See Samson et al. (1996), page 3364, Fig. 1 and right col. Applicants note, further, that these extracellular domains necessarily represent the structural determinants and epitopes to which anti-CCR5 antibodies that inhibit CCR5-mediated fusion to HIV-1 bind. Since these extracellular domains had been publicly described, it was not necessary for compliance with the written description requirement, to disclose them in the specification. M.P.E.P. §2163(II)(2) states that in analyzing whether the specification complies with the written description requirement, "[i]nformation which is well known in the art need not be described in detail in the specification."

Moreover, applicants maintain that knowledge of CCR5 epitopes or any other structural determinants of the human CCR5 receptor that might prove to be suitable targets for a fusion-inhibitory antibody is not necessary to adequately describe antibodies that bind to the receptor on the surface of a CD4+ cell and inhibit CCR5-mediated fusion with HIV-1. This is because antibodies with the specified properties can be produced, identified, and described, without any knowledge of the CCR5 epitopes to which such antibodies bind. Such antibodies can be produced and identified by routine experiments involving immunizing an animal with cells expressing the CCR5 receptor on their surface, and screening the

antibodies thereby generated using the RET assay to identify those that inhibit fusion of HIV-1 to CD4+ CCR5+ cells.

As noted by the Examiner, an issue of lack of adequate written description arises if the specification does not describe the claimed subject matter in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. However, applicants contend that in an art characterized by high skill, the level of disclosure required to satisfy the written description requirements is less that would be required if the level of skill in the art was low. In support of this position, applicants respectfully direct the Examiner's attention to M.P.E.P. §2163(II)(2) which states that "[g]enerally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement." Applicants have noted above that the level of skill in the biotechnology arts is high. Applicants assert that in the instant case, the high level of skill in the art is a favorable factor in assessing the sufficiency of the written description, and maintain that the claimed invention is adequately described in the specification.

Applicants maintain that the above-identified disclosures in the specification pertaining to an antibody which binds to a human CCR5 chemokine receptor on the surface of a CD4+ cell and inhibits HIV-1 infection of such CD4+ cell suffice to convey to a person skilled in the art that applicants were in possession of the claimed invention at the time the specification was filed. Accordingly, applicants maintain that the specification as filed satisfies the written description requirement of 35 U.S.C. §112, first paragraph, with regard to the now-pending claims.

In view of the remarks set forth above, applicants respectfully request that the Examiner reconsider and withdraw the rejections set forth in the September 7, 2005 Office Action, and solicit allowance of all claims pending in the subject application.

Supplemental Information Disclosure Statement

This Supplemental Information Disclosure Statement is submitted under 37 C.F.R. §1.97(c)(2) to supplement the Information Disclosure Statements filed on August 9, 2001, June 6, 2002, March 26, 2003, April 16, 2003 and September 7, 2004 in connection with the subject application.

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are listed on the attached Form PTO-1449 (**Exhibit B**), and certain of which are attached hereto as **Exhibits 1-27,** respectively:

1. U.S. Patent No. 6,265,184, issued to P.W. Gray et al. on July 24, 2001;

2. U.S. Patent No. 6,268,477, issued to P.W. Gray et al. on July 31, 2001;

3. U.S. Patent No. 6,797,811, issued to P.W. Gray et al. on September 28, 2004;

4. U.S. Patent No. 6,800,729, issued to Y. Li et al. on October 5, 2004;

5. U.S. Patent No. 6,511,826, issued to Y. Li et al. on January 28, 2003;

6. U.S. Patent No. 6,743,594, issued to Y. Li et al. on June 1, 2004;

7. U.S. Patent No. 6,025,154, issued to Y. Li et al. on October 5, 2004;

8. U.S. Patent No. 6,448,375, issued to M. Samson et al. on September 10, 2002;

9. U.S. Patent No. 6,692,938, issued to M. Samson et al., February 17, 2004;

10. U.S. Patent No. 6,800,447, issued M. Samson et al., October 5, 2004;

11. Y. Li et al., U.S. Publication No. 2001/0000241 Al, published April 12, 2002;

12. Y. Li. et al., U.S. Publication No. 2004/0151719, published August 8, 2004;

13. C.A. Rosen et al., U.S. Publication No. 2003/0166024 Al, published September 4, 2003;

14. C.A. Rosen et al., U.S. Publication No. 2002/0061834 Al, published May 23, 2002;

15. C.A. Rosen et al., U.S. Publication No. 2002/0048786 Al, published April 25, 2002;

16. P.W. Gray et al., U.S. Publication No. 2002/0150888 Al, published October 17, 2002;

17. P.W. Gray et al., U.S. Publication No. 2004/0230037 A1, published November 11, 2004;

18. M. Samson et al., U.S. Publication No. 2004/0161739 A1, published August 19, 2004;

19. M. Samson et al., U.S. Publication No. 2004/0110127 A1, published June 10, 2004;

20. V. Roschke et al., U.S. Publication No. 2005/0154193 A1, published July 14, 2005;

21. V. Roschke et al., U.S. Publication No. 2003/0100058 A1, published May 29, 2003;

22. PCT International Publication WO 01/58915, published August 16, 2001 **(Exhibit 1)**;

23. PCT International Publication WO 01/58916, published August 16, 2001 **(Exhibit 2)**;

24. PCT International Publication No. WO 96/39437, published December 12, 1996 **(Exhibit 3)**;

25. PCT International Publication No. WO 97/22698, published in June 26, 1997 **(Exhibit 4)**;

26. PCT International Publication No. WO 97/032019, published in September 4, 1997 **(Exhibit 5)**;

27. PCT International Publication No. WO 02/064612, published August 22, 2002 **(Exhibit 6)**;

28. PCT International Publication WO 97/44055, published November 27, 1997 **(Exhibit 7)**;

29. European Application No. EP 96870102.9, filed August 6, 1996 **(Exhibit 8)**;

30. European Application No. EP 96870021.1, filed March 1, 1996 **(Exhibit 9)**;

31. CA 19972216990, published November 27, 1997 **(Exhibit 10)**;

32. European Publication No. EP 0815137, published January 1, 1998 **(Exhibit 11)**;

33. European Publication No. EP 1199360, published April 24, 2 002 **(Exhibit 12)**;

34. European Publication No. EP 1145721, published October 17, 2001 **(Exhibit 13)**;

35. European Publication No. EP 1146055, published October 17, 2001 **(Exhibit 14)**;

36. European Publication No. EP 1146122, published October 17, 2001 **(Exhibit 15)**;

37. European Publication No. EP 1148126, published October 24, 2001 **(Exhibit** 16);

38. European Publication No. EP 1148127, published October 24, 2001 **(Exhibit 17)**;

39. European Publication No. EP 1149582, published October

31, 2001 **(Exhibit 18)**;

40. European Publication No. EP 1482042, published December 1, 2004 **(Exhibit 19)**;

41. European Publication No. EP 0883687 B1, published December 16, 1998 **(Exhibit 20)**;

42. Strawman Limited, European Opposition Against Euroscreen, June 27, 2005 **(Exhibit 21)**;

43. Dean, M. et al. (1996) Genetic restriction of HIV-1 infection and progressionto AIDS by a deletion allele of the CKR5 structural gene,Science 273: 1856-1862 **(Exhibit 22)**;

44. He, Jianglin et al. (1997) CCR3 and CCR5 are co-receptors for HIV-1 infection of microglia, Nature 385: 645-649 **(Exhibit 23)**;

45. Mackay, C.R. (1996) Chemokine receptors and T cell chemotaxis, J. Exp. Med. 184: 799-802 **(Exhibit 24)**;

46. Raport, C.J. et al. (1996) Molecular cloning and functional characterization of a novel human CC Chemokine Receptor (CCR5) for RANTES, MIP-1(3, and M1P-la, J. Biol. Chem. 271: 17161-17166 **(Exhibit 25)**;

47. Samson, M. et al. (1996) Molecular cloning and functional expression of a new human CC-Chemokine receptor gene, Biochem. 35: 3362-3367 **(Exhibit 26)**; and

48. Wu, L. et al., CD4-induced interaction of primary HIV-1

gp120 glycoproteins with the chemokine receptor CCR-5, Nature 384: 179-183 **(Exhibit 27)**.

The Examiner is respectfully requested to make these references of record in the present application by initialing and returning a copy of the enclosed Form PTO 1449.

Pursuant to 37 C.F.R. §1.98(a)(2), as amended in the September 21, 2004 Final Rule, copies of U.S. Patents and U.S. Patent Application Publications must not be submitted. Accordingly, copies of references 1-10 (U.S. Patents) and reference 11-21 (U.S. Patent Application Publications) are not attached hereto.

If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

Pursuant to 37 C.F.R. §1.97(c)(2) and 1.17(p), a fee of one hundred and eighty dollars ($180.00) is required for filing the enclosed Supplemental Information Disclosure Statement. A fee of five hundred and ten dollars ($510.00) is also required for a three-month extension of time for responding to the September 7, 2005 Office Action. Pursuant to 37 C.F.R. §1.321(c) and 1.20(d), a fee of sixty-five dollars ($65.00) is required for filing the attached Terminal Disclaimer. Accordingly, a check in the total amount of six hundred and ninety dollars ($755.00) is enclosed. If any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
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Date